The Threat of Pandemic Influenza

What is Influenza?

Influenza is caused by a virus that attacks the upper respiratory tract–the nose, throat, and bronchi, and, rarely, the lungs. The infection is characterized by a sudden onset of fever, myalgia, headache, nonproductive cough, sore throat, and rhinitis about one to four days after exposure. Influenza is transmitted by droplets and droplet nuclei released after infected persons cough or sneeze. Adults are typically infectious from one day prior to five days after illness onset. Children can be infectious for over 10 days, and can shed virus up to six days prior to illness onset. Most people recover within one to two weeks without requiring medical treatment. Hospitalization and deaths mainly occur in high-risk groups, such as the elderly and immunosuppressed.

The hallmark feature of influenza viruses is their ability to mutate. All influenza viruses have a segmented genome, which can rearrange to produce new viral proteins. These new proteins result in new strains of virus. Influenza viruses are categorized as type A, B, or C. Types B and C are found in humans. Type B causes mild to moderately severe illness, whereas type C causes mostly asymptomatic infection. However, type A can infect humans **and** animals, such as birds (including poultry and ducks) and pigs. Influenza A viruses can be further divided into subtypes according to differences between two viral surface proteins, hemagglutinin (H) and neuraminidase (N). There are 16 H antigens (H1-H16) and 9 N antigens (N1-N9).

What is Pandemic Influenza?

There are two ways an influenza virus can mutate. A regular, small, and permanent change in the genetic material of the virus is known as **antigenic drift**. This creates seasonal epidemics and is why a flu vaccine developed for the last flu season will not protect against the new strain of the current season. Because the body lacks specific antibodies for the new strain, there is incomplete natural protection.

A virus may also mutate through a process known as **antigenic shift**. This occurs when two or more influenza A subtypes from different species–such as bird and pig or bird and human–trade and merge genes, creating a new combination of H and N proteins. This results in a new, or novel, virus to which humans have not been exposed. The general population would have little or no immunity, and a pandemic (worldwide epidemic) causing widespread illness and death is possible. Three pandemics occurred in the twentieth century (see table below). The last two pandemic viruses were combinations of bird and human influenza viruses.

To cause a pandemic, a viral strain must have three characteristics:

- Be **novel** to the human population;
- Have **increased virulence**, resulting in high morbidity and mortality; and
- Be **easily transmitted** human to human.

Why Are Public Health Officials Concerned Now?

Recently, there has been an outbreak of avian (bird) influenza A H5N1 in chickens in Vietnam, Thailand, and Cambodia. This highly pathogenic strain is generally transmitted from bird to bird. Migratory birds, such as wild ducks, are often asymptomatic carriers of viruses which then transmit the virus to domestic fowl such as chickens, turkeys, and geese. These domestic species, which, in Asia, generally live in close proximity to humans and domestic animals, are highly susceptible.

Influenza A H5N1 does not generally affect humans; however, this outbreak has caused several human infections, with an approximate 50 percent mortality rate for the reported cases. This strain is often accompanied by primary viral pneumonia and acute respiratory distress, the most common cause of flu-related death. Most cases occurred from direct contact with infected poultry or wild ducks. Although very few cases are believed to have occurred from close human-to-human contact with infected cases, further viral mutation may result in easy human-to-human transmission. Health officials fear that this strain or another strain may possibly cause the next influenza pandemic.

Laboratory Diagnosis

Influenza is difficult to distinguish from other respiratory illnesses by clinical diagnosis alone. Laboratory testing is necessary to confirm a diagnosis and identify circulating strains. This will be especially critical in tracking the emergence and transmission of a pandemic strain.

Prevention and Treatment

Vaccination is the principal measure for preventing influenza and reducing the impact of epidemics. Vaccines are based on previously circulating strains. However, since a pandemic strain would be a newly recognized strain, a vaccine would not be available for several months. Oseltamivir (TamiFlu™) is the only drug approved by the U.S. Food and Drug Administration that is effective for the treatment and prevention of the H5N1 strain circulating in Southeast Asia. Supplies will likely be extremely limited during the initial phases of a pandemic.

In the absence of a vaccine and effective antivirals, proper infection control measures, such as hand washing, covering mouths when coughing and sneezing, discarding used tissues, and staying home from work and school if ill, will be critical in preventing the transmission of pandemic influenza.

What's Next?

No one can predict when the next pandemic will occur, or if the circulating H5N1 strain will cause a pandemic. However, federal, state, and local health officials are developing plans and training initiatives to prepare for the next influenza pandemic. The Indiana State Department of Health (ISDH) has developed the Indiana Pandemic Influenza Preparedness Plan, currently under review. This plan will be submitted to the Centers for Disease Control and Prevention by August 25, 2005, and distributed to internal and external partners. The ISDH is also providing pandemic influenza training within the public health preparedness districts this summer and distributing information to health care providers.

Influenza Pandemics of the 20th Century: Impact in the United States*			
Date	**Strain**	**Estimated No. of Deaths in US**	**Comments**
1918-1919 (Spanish Flu)	H1N1	500,000	Global mortality may have been as high as 100 million. The virus likely originated in the U.S. and then spread to Europe.
1957-58 (Asian Flu)	H2N2	60,000	The virus was first identified in China. Approximately 1 million people died globally during this pandemic.
1968-69 (Hong Kong Flu)	H3N2	40,000	The death rate from this pandemic may have been lower, because the strain had a shift in the hemagglutinin (H) antigen only and not in the neuraminidase (N) antigen.
*All three pandemics were characterized by a shift in age distribution of deaths to younger population under age 65 (at least initially); shift was particularly dramatic during 1918 pandemic (see References: NIH: Focus on the flu; HHS: Influenza pandemics; Simonsen 2004; Webster 1997).			